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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,417

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Shinzo Yasuda

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EXAMINER

LONG, SCOTT

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

10/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,417	Applicant(s) YASUDA ET AL.	
	Examiner Scott D. Long	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9,11-13 and 26-34 is/are pending in the application.
- 4a) Of the above claim(s) 8,9,12,13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11 and 26-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/19/2008 & 10/7/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/20/2008 has been entered.

Election/Restrictions

Applicant's election with traverse of Group III (claims 11, 26-28 and 30-33) in the reply filed on 7/16/2008 is acknowledged. The applicant has traversed the examiner's restriction on several grounds.

As the instant application is a National Stage Application of PCT/JP05/05480, the examiner is required to review the claims according to PCT Rule 13.1. According to Rule 13.1, an "international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept." The examiner had previously indicated (Restriction Requirement, filed 6/17/2008) that the claims have evolved during the course of prosecution, such that there are now three structurally distinct bacteria being claimed. Furthermore, there are three distinct methods also

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claimed, respectively requiring different reagents (namely, the structurally distinct bacteria). The examiner reasoned that there could not be a special technical feature that unites all of these inventions because there are three distinct methods, using three distinct reagents to produce the same product (1,3-propanediol and 3-hydroxypropionic acid) from an identical carbon source (glycerol). The restrictions based on Lack of Unity have a different requirement for restriction than those based upon typical U.S. Utility Application Restriction practice.

The applicant traverses the examiner's restriction requirement, as though it were a restriction based on normal US restriction practice, stating that (1) are classified in the same class and subclass, (2) were previously examined together, and (3) searching would not cause undue burden to the examiner. The examiner does not believe these are germane to the National Stage restrictions, but fully disagrees with the thrust of these arguments, because the USPTO classification system is extremely limited for some technologies, particularly recombinant bacteria. There is nothing in the current classification system that allows the examiner to satisfactorily separate the myriad variety of recombinant bacteria from each other, even though they might contain different genetic mutations, gene knockouts, or exogenous gene insertions. So, structurally distinct transgenic microorganisms might have the same classification, but nevertheless be fundamentally distinct inventions. Furthermore, under the applicant's logic, all microorganisms which utilize the same carbon source and produce the same metabolite would share the same technical feature. Such a generalization would imply there is no inventive concept. The examiner finds this reasoning fallacious. Regarding

the applicant's assertion that there is no search burden for the examiner, the Examiner can assure the applicant that searching for a microorganism having a unique set of gene deletions and insertions will not necessarily identify a microorganism having a different set of gene deletions and insertions. It would be burdensome to search for multiple different transgenic microorganisms.

Finally, the applicant attempts to address the examiner's assertion that there is no special technical feature and requests co-examination of groups I & IV, or II & V, or III & VI. While the applicant asserts that all groups share a special technical feature, the applicant fails to identify this special technical feature. Instead, the applicant states that the pairs of groups, cited above, each share a special technical feature of a distinct knockout bacteria (e.g., "Groups I and IV share the special technical feature of the knockout bacteria of claim 8" (Remarks, page 3)). The applicant further argues, that since examining any of Groups IV, V, or VI would require the search of Groups I, II, or III, respectively. The applicant, therefore, reasons that the pairs of groups form a single general inventive concept and satisfy the requirement for unity of invention under PCT Rule 13.1. Unfortunately, the examiner takes the applicant's arguments as reaffirming the examiner's belief that there are three distinct products and three distinct methods among the pending claims. The fact that each method requires a different bacterium, support the proposition that each method does not share a common technical feature with the other two methods. As for examining the pairs of Groups together, the examiner does not find there is a special technical feature uniting all claims and

therefore finds that there cannot be unity of invention. Accordingly, the examiner finds the applicant's arguments unpersuasive.

However, despite the fact that the examiner believes there is a lack of unity between the 6 groups, while searching for the elected group III, the examiner was able to find limitations directed to the corresponding method of group VI. Therefore, the examiner has examined both Groups III and VI.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Claim Status

Claims 8-9, 11-13 and 26-34 are pending. Claims 1-7, 10 and 14-25 are cancelled. Claims 8-9 and 11-13 are amended. Claims 26-34 are newly submitted. Claims 8, 9, 12, and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/16/2008. Claims 11 and 26-34 are under current examination.

Priority

This application claims benefit as a 371 of PCT/JP05/05480 (filed 03/25/2005). This application also claims benefit from foreign patent applications JAPAN 2004-093417 (filed 03/26/2004) and JAPAN 2004-124524 (filed 04/20/2004). The instant application has been granted the benefit date, 26 March 2004, from the application JAPAN 2004-093417.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 6/19/2008 and 10/7/2008 consisting of 2 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Response to Arguments - Claim Objections

Applicant's arguments (Remarks, page 6) and Claim amendments, filed 19 June 2008, with respect to claims 2-10 have been fully considered and are persuasive. The objections to Claims 2-10 based on failing to further limit a previous claim have been made moot by the claim amendments submitted on 19 June 2008 and are hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – WRITTEN DESCRIPTION

The rejection of claims 11 and 14-25 under 35 USC 112, 1st paragraph are withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, pages 9-10, filed 6/19/2008) and claim amendments have been fully considered and they are persuasive. The applicant has amended the claims so that specific SEQ ID NOs have been used to identify the various genes inserted into the transgenic microorganism. Accordingly, there is no lack of written description.

Therefore, the examiner hereby withdraws the rejection of claims 11 and 14-25 under 35 USC 112, 1st paragraph.

Response to Arguments - Claim Rejections 35 USC § 102

The rejection of claim 11 under 35 USC 102(b) as anticipated by Ahrne et al. (Current Microbiology. 1992; Vol.24: 199-205) is withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, page 10, filed 6/19/2008) and claim amendments have been fully considered and they are persuasive. The applicant has amended the claims so specifically, that the cited art does not anticipate the instant claim.

Therefore, the examiner hereby withdraws the rejection of claim 11 under 35 USC 102(b) as anticipated by Ahrne et al.

The rejection of claim 10-11 and 2-7 under 35 USC 102(e) as anticipated by Laffend et al. (US-7,135,309) is withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, pages 10-11, filed 6/19/2008) and claim amendments have been fully considered and they are persuasive. Claims 10 and 2-7 are cancelled, so rejection of these claims is moot. The applicant has amended the claim 11 so specifically, that the cited art does not anticipate the instant claim.

Therefore, the examiner hereby withdraws the rejection of claim 11 under 35 USC 102(e) as anticipated by Laffend et al.

Response to Arguments - Claim Rejections 35 USC § 103

The rejection of claims 2-7 and 10-11 under 35 USC 103(a) as unpatentable over Skraly et al. (US-6,329,183) in view of Dobrogosz et al. (US-5,352,586) is withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, page 15-16, filed 6/19/2008) and claim amendments have been fully considered and they are persuasive. This rejection is directed to withdrawn claims, 8-9 and 12-13. Therefore, the rejection is moot.

Accordingly, the examiner hereby withdraws the rejection of claims 2-7 and 10-11 under 35 USC 103(a) as unpatentable over Skraly et al. in view of Dobrogosz et al.

The rejection of claims 8-9 and 12-13 under 35 USC 103(a) as unpatentable over Nair et al. (US-7,005,291) is withdrawn in response to the applicant's arguments and/or claim amendments.

Applicant's arguments (Remarks, page 15-16, filed 6/19/2008) and claim amendments have been fully considered and they are persuasive. This rejection is directed to withdrawn claims, 8-9 and 12-13. Therefore, the rejection is moot.

Accordingly, the examiner hereby withdraws the rejection of claims 8-9 and 12-13 under 35 USC 103(a) as unpatentable over Nair et al.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Kandler et al. 1980. *Lactobacillus reuteri* sp. nov. a new species of heterofermentative lactobacilli. *Zbl. Bakt. Hyg. Abt. Orig. C1*:264-269).

Claim 11 is directed to a transformant of *Lactobacillus reuteri* comprising genes introduced from *Lactobacillus reuteri*.... The scope of claim 30 is identical to claim 11, but recites polynucleotide SEQ ID NOs, rather than polypeptide SEQ ID NOs. The instant specification does not define the term “transformant.” Therefore, the examiner broadly interprets the phrase “a transformant of *Lactobacillus reuteri* comprising genes introduced from *Lactobacillus reuteri*” to mean an isolated *Lactobacillus reuteri*. The examiner interprets the phraseology regarding “transformant” to mean that genes of *Lactobacillus reuteri* were transferred between generations of *Lactobacillus reuteri* over the course of evolution. The instant specification teaches that all of the specific SEQ ID NOs recited in the instant claims are from the wild type *Lactobacillus reuteri* microorganism and have not been modified. Because Kandler et al. teach an isolated *Lactobacillus reuteri*, the examiner believes all the limitations of the instant claims are inherently met by Kandler et al.

Accordingly, Kandler et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11 and 26-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nair et al. (US-7,005,291, issued 28 February 2006) in view of Talarico et al. (Applied and Environmental Microbiology. Apr.1990; 943-948).

Claims 11 and 30 are directed to a transformant of *Lactobacillus reuteri* comprising genes introduced from *Lactobacillus reuteri*...[having SEQ ID NOs which correspond to naturally occurring genes encoding the following proteins from *Lactobacillus reuteri*: large, medium, and small subunits of glycerol dehydratase; large and small subunits of a reactivation factor for glycerol dehydratase; propionaldehyde dehydrogenase; propanol dehydrogenase].

Claim 26 and 31 are directed to the transformant claim 11 and claim 30, respectively, which is lacking glycerol dehydrogenase gene, but contains phosphotransacylase and propionate kinase genes. Claim 27 and 33 are directed to limiting the *Lactobacillus reuteri* transformant, so that the transformant must contain where a naturally occurring propionate kinase gene/protein of particular SEQ ID NOs. Claims 28 and 32 are directed to further limiting the *Lactobacillus reuteri* transformant, so that the transformant must also contain the pdu Operon. *Lactobacillus reuteri* inherently contains the Phosphate acetyltransferase gene and pdu operon. Nair et al. teach, "recombinant host having disruptions in genes encoding endogenous glycerol dehydrogenase enzymes (col.5, lines 13-16). Nair et al. teach, "glycerol dehydrogenase protein, the product of gldA, is produced in the [E.coli] transformants.... Of 8 transformants analyzed, 6 were determined to be gldA knockouts" (col.24, lines 55-67). Nair et al. teach "a recombinant organism comprising...a disruption in one or both

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of (a) a gene encoding an endogenous glycerol kinase and (b) a gene encoding a endogenous glycerol dehydrogenase." (col.3, line 63 to col.4, line 6). Nair et al. teach "bacterial strains able to produce 1,3-propanediol have been found, for example, in the groups... *Lactobacillus*" (Col.2, lines 55-58). Nair et al. also suggests the general concept of the cells transformed with heterologous genes suitable for the production of 1,3-propanediol" (col.4, lines 13-29).

Claims 29 and 34 are directed to methods of producing 1,3-propanediol and β -hydroxypropionic acid, using the transformants of claims 11 and 30, respectively. Nair et al. teach a "process...for a recombinant organism...in a host cell having disruptions in the endogenous ...dehydrogenase genes...[a]pplicant's process may generally applied to the production [of] compounds where glycerol is a key intermediate, e.g., 1,3-propanediol" (col.5, lines 23-30). Nair et al. teach "a process for production of 1,3-propanediol from a recombinant organism comprising...a disruption in one or both of (a) a gene encoding an endogenous glycerol kinase and (b) a gene encoding a endogenous glycerol dehydrogenase." (col.3, line 63 to col.4, line 6). Nair et al. also suggests the general concept of the cells transformed with heterologous genes suitable for the production of 1,3-propanediol" (col.4, lines 13-29).

Nair et al. does not specifically teach that their methods and organisms can utilize the species *Lactobacillus reuteri*, although they suggest that species of the *Lactobacillus* genus could be used.

However, Talarico et al. teach that *Lactobacillus reuteri* grown in the presence of glycerol can be used to produce 1,3-propanediol and 3-hydroxypropionic acid.

Accordingly, Talarico et al. suggest that *Lactobacillus reuteri* contain all the genes required by the instant claims.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to use the teachings of Nair et al. and Talarico et al. to generate a transformant of *Lactobacillus reuteri* comprising a knocked out glycerol dehydrogenase gene to produce 1,3-propanediol and 3-hydroxypropionic acid.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (*Lactobacillus reuteri* comprising the genes recited in the instant claims; and recombinant production of to produce 1,3-propanediol and 3-hydroxypropionic acid by recombinant host having disruptions in genes encoding endogenous glycerol dehydrogenase enzymes) are taught by Nair et al. or Talarico et al.

In addition, Nair et al. also suggest cells transformed with heterologous genes suitable for the production of 1,3-propanediol" (col.4, lines 13-29). It would seem that a transgenic *Lactobacillus reuteri* comprising the genes from wildtype *Lactobacillus reuteri* would be obvious over a wild type *Lactobacillus reuteri* comprising the same genes, there being so particular difference between the two microorganisms except that genetic manipulation has performed on the former. In addition, while instant claims 26 and 31

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recite the limitation “not any glycerol dehydrogenase gene,” this lack of a functional glycerol dehydrogenase gene would seem to be an obvious equivalent of the glycerol dehydrogenase gene knockouts suggested by Nair et al.

An artisan would have expected success, because methods of making transgenic bacteria are well known in the art.

Therefore the method and knockout microorganism as taught by Nair et al. in view of Talarico et al. would have been *prima facie* obvious over the method and transformant of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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